

Session 1: Diagnosis of Stable Ischemia and CHD

1. Physiologic techniques & their relation to structure - Flow & endothelium: Carl J. Pepine, M.D.

2. Where we stand in 2002 – Overview/Rationale

The majority of women referred to coronary angiography for symptoms suggesting cardiac ischemia have “normal angiograms” or no flow limiting stenoses. While minimal lesions have been recognized as a substrate for acute coronary syndromes, these women are known to have relatively good outcomes in terms of acute coronary syndromes (death and MI) over the intermediate term (approximately three years). Since CHD is known to be delayed in its more serious expression (death and MI) by ~12 years in women compared with men, the limited follow-up data are insufficient to assure that these symptoms are not an early expression of CHD. Furthermore, it is known that many of these women have poor quality of life due to recurrent symptoms that prompt frequent physician and hospital visits, repetitive testing and disability.

Could these symptoms result from ischemia due to coronary vascular findings other than flow-limiting lesions in the large vessels? To this end, coronary flow and endothelial function have been evaluated in detail in a subset of women in the WISE. Intravascular ultrasound was also done to determine whether these physiologic findings are linked with structural changes in the arterial wall of the large coronary arteries.

These data suggest that the majority of women in the WISE without flow-limiting lesions tested have abnormalities of coronary endothelial function and/or microvascular flow reserve. In many instances, these abnormalities are of such severity that they have the potential to limit coronary perfusion. Additionally, the WISE IVUS substudy has identified evidence for extensive atherosclerotic plaque in over 80% of women studied to date. While the plaque indices are highly correlated with traditional atherosclerosis risk factors and the endothelial dysfunction, the links with microvascular findings are not yet clear.

3. Current challenges and most important issues for future research

Identify links between disordered coronary function (endothelial dysfunction and microvascular flow limitations) and structure (IVUS determined plaque and remodeling indices).

Evaluate links between traditional atherosclerosis risk factors and disordered coronary function (endothelial dysfunction and microvascular flow limitations) and structure (IVUS determined plaque and remodeling indices).

Determine intermediate/long-term prognosis for women with coronary vascular dysfunction in the absence of flow limiting large vessel stenosis.

Study mechanisms responsible for disordered coronary function (endothelial dysfunction and microvascular flow limitations) and structure (IVUS determined plaque and remodeling indices).

4. Current challenges in communicating messages to health care community, patients and the public

Awareness that absence of flow limiting lesions on coronary angiography is not necessarily a benign condition. Unfortunately many women with these findings are denied even traditional atherosclerosis prevention.

Recognition that patients without flow limiting stenosis may have disorders of coronary function.

Need for more research into mechanisms and treatments of these disorders in women.

5. Translating new findings to improve diagnosis and treatment

This will require a large RCT to determine whether a strategy employing additional tests for coronary dysfunction and subsequent treatments directed at this dysfunction results in better outcomes than a strategy of usual care (not testing).